Claims

1. A method for detecting the methylation state of the 5' and promoter region of the gene DD3 within a subject, said method comprising contacting a target nucleic acid comprising one or more sequences from the group of Seq. ID No.1 to Seq. ID No. 5 in a biological sample obtained from said subject with at least one reagent or a series of reagents, wherein said reagent or series of reagents, distinguishes between methylated and non methylated CpG dinucleotides within the target nucleic acid.

2. A method for the analysis of cell proliferative disorders, comprising determination of the methylation state of one or more sequences from the group of Seq. ID No.1 to Seq. ID No. 5 according to Claim 1.

3. A method according to Claim 2, wherein the biological sample is prostate cells or derived from prostate cells.

4. A nucleic acid molecule comprising a sequence at least 18 bases in length according to one of the sequences taken from the group comprising Seq. ID No. 1 to Seq. ID No. 5 and sequences complementary thereto.

5. An oligomer, in particular an oligonucleotide or peptide nucleic acid (PNA)-oligomer, said oligomer in each case consisting essentially of at least one base sequence having a length of at least 10 nucleotides which hybridises to or is identical to one of the nucleic acid sequences according to Seq. ID No. 1 to Seq. ID No. 5.

6. An oligomer as recited in Claim 5, consisting essentially of one of the sequences taken from the group of Seq. ID No. 6 to Seq. ID No. 92.

7. The oligomer as recited in Claim 5, wherein the base sequence includes at least one CpG dinucleotide.

8. The oligomer as recited in Claim 7, characterised in that the cytosine of the CpG dinucleotide is located approximately in the middle third of the oligomer.

9. A set of oligomers, comprising at least two oligomers according to any of claims 5 to 8.

10. A set of oligomers as recited in Claim 9, comprising oligomers for detecting the methylation state of all CpG dinucleotides within Seq. ID No. 1 and sequences complementary thereto.

11. A set of at least two oligonucleotides as recited in one of Claims 5 to 10, which is used as primer oligonucleotides for the amplification of DNA sequences of one of Seq. ID No. 1 to Seq. ID No. 5 and sequences complementary thereto.

12. A set of oligonucleotides as recited in one of Claims 9 or 11, characterised in that at least one oligonucleotide is bound to a solid phase.

13. Use of a set of oligonucleotides comprising at least three of the oligomers according to any of claims 5 through 12 for detecting the cytosine methylation state and/or single nucleotide polymorphisms (SNPs) within the sequences taken from the group of Seq. ID No. 1 to Seq. ID No. 5 and sequences complementary thereto.

14. A method for manufacturing an arrangement of different oligomers (array) fixed to a carrier material for analysing diseases associated with the methylation state of the CpG dinucleotides of the gene DD3, wherein at least one oligomer according to any of the claims 5 to 12 is coupled to a solid phase.

15. An arrangement of different oligomers (array) obtainable according to claim 14.

16. An array of different oligonucleotide- and/or PNA-oligomer sequences as recited in Claim 15, characterised in that these are arranged on a plane solid phase in the form of a rectangular or hexagonal lattice.

17. The array as recited in any of the Claims 15 or 16, characterised in that the solid phase surface is composed of silicon, glass, polystyrene, aluminium, steel, iron, copper, nickel, silver, or gold.

18. A DNA- and/or PNA-array for analysing diseases associated with the methylation state of the gene DD3 comprising at least one nucleic acid according to one of the preceding claims.

19. A method for determining the methylation state within at least one nucleic acid molecule according to one of Seq. ID No. 1 to Seq. ID No. 5, characterised in that the following steps are carried out:
a) obtaining a biological sample containing genomic DNA,
b) extracting the genomic DNA,
c) converting cytosine bases which are unmethylated at the 5-position within said DNA sample, by chemical treatment, to uracil or another base which is dissimilar to cytosine in terms of hybridisation behaviour;
d) amplifying fragments of the chemically pretreated genomic DNA using sets of primer oligonucleotides according to one of Claims 11 or 12 and a polymerase, and
e) identifying the methylation status of one or more cytosine positions.

20. The method as recited in Claim 19, characterised in that Step e) is carried out by means of hybridisation of at least one oligonucleotide according to Claims 5 to 12.

21. The method as recited in Claim 19, characterised in that Step e) is carried out by means of hybridisation of at least one oligonucleotide according to Claims 5 to 12 and extension of said hybridised oligonucleotide(s) by means of at least one nucleotide base.

22. The method as recited in Claim 19, characterised in that Step e) is carried out by means of sequencing.

23. The method as recited in Claim 19, characterised in that Step d) is carried out using methylation specific primers.

24. The method as recited in Claim 19, characterised in that Step e) is carried out by means of a combination of at least two of the methods described in Claims 20 to 23.

25. The method as recited in Claim 19, characterised in that the chemical treatment is carried out by means of a solution of a bisulfite, hydrogen sulfite or disulfite.

26. A method for the analysis of methylation within a nucleic acid molecule comprising Seq. ID No. 1 comprising the following steps;
    a) obtaining a biological sample containing genomic DNA,
    b) extracting the genomic DNA,
    c) digesting the genomic DNA comprising Seq. ID No. 1 with one or more methylation sensitive restriction enzymes, and
    d) detection of the DNA fragments generated in the digest of step c).

27. A method according to Claim 26, wherein the DNA digest is amplified prior to Step d).

28. The method as recited in one of the Claims 19 to 25 and 27 characterised in that more than ten different fragments having a length of 100 - 2000 base pairs are amplified.

29. The method as recited in one of Claims 19 to 25, 27 and 28 characterised in that the amplification of several DNA segments is carried out in one reaction vessel.

30. The method as recited in one of the Claims 19 to 25 and 27 to 29, characterised in that the polymerase is a heat-resistant DNA polymerase.

31. The method as recited in claims 19 to 25 and 27 to 30, characterised in that the amplification is carried out by means of the polymerase chain reaction (PCR).

32. The method as recited in one of the Claims 19 to 25 and 27 to 31, characterised in that the amplificates carry detectable labels.

33. The method according to Claim 32 wherein said labels are fluorescence labels, radionuclides and/or detachable molecule fragments having a typical mass which can be detected in a mass spectrometer.

34. The method as recited in one of the Claims 19 to 25, characterised in that the amplificates or fragments of the amplificates are detected in the mass spectrometer.

35. The method as recited in one of Claims 33 or 34, characterised in that the produced fragments have a single positive or negative net charge for better detectability in the mass spectrometer.

36. The method as recited in one of Claims 33 to 35, characterised in that detection is carried out and visualised by means of matrix assisted laser desorption/ionisation mass spectrometry (MALDI) or using electron spray mass spectrometry (ESI).

37. The method as recited in one of the Claims 19 to 32, characterised in that the genomic DNA is obtained from cells or cellular components which contain DNA, sources of DNA comprising, for example, cell lines, histological slides, biopsies, tissue embedded in paraffin and all possible combinations thereof.

38. A kit comprising a bisulfite (= disulfite, hydrogen sulfite) reagent as well as oligonucleotides and/or PNA-oligomers according to one of the Claims 5 to 13.

39. A kit according to claim 38, further comprising standard reagents for performing a methylation assay from the group consisting of MS-SNuPE, MSP, Methyl light, Heavy Methyl, nucleic acid sequencing and combinations thereof.

40. The use of a method according to one of claims 1 to 3, 14, and 19 to 37, a nucleic acid according to Claims 3 to 4, of an oligonucleotide or PNA-oligomer according to one of the Claims 5 to 8, of a kit according to Claim 38 or 39, of an array according to one of the Claims 15 to 18 or of a set of oligonucleotides according to one of claims 9 to 13 for the characterisation, classification, differentiation, grading, staging, and/or diagnosis of cell proliferative disorders, or the predisposition to cell proliferative disorders.

41. The use of a method according to one of claims 1 to 3, 14, and 19 to 37, a nucleic acid according to Claims 3 to 4, of an oligonucleotide or PNA-oligomer according to one of the Claims 5 to 8, of a kit according to Claim 38 or 39, of an array according to one of the Claims 15 to 18 or of a set of oligonucleotides according to one of claims 9 to 13 for the therapy of cell proliferative disorders.